IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	PENDHARKAR, Sanyog M.	Confirmation No.	6658
Serial No.:	10/567,388	Art Unit:	1651
Filed:	February 7, 2006	Examiner:	WARE, Deborah K.
For:	HEMOSTATIC COMPOSITIONS CONTAINING STERILE THROMBIN		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR PRE-APPEAL BRIEF HEARING

Dear Sir:

In response to the Advisory Action to be issued March 27, 2009 (pursuant to a call to the Examiner on even date herewith), and the Final Rejection issued November 26, 2008, Applicants submit the following Request for a Pre-Appeal Brief Hearing. A Notice of Appeal and a petition for one (1) month extension of time are filed concurrently herewith.

REMARKS

Claims 1-13 stand rejected under 35 U.S.C. §102(b) as being anticipated by Reich et al. (U.S. Published Application No. 2002/0042378). Applicants traverse this basis for rejection and respectfully request reconsideration and withdrawal thereof.

The present claims are directed to a sterile hemostatic composition of a continuous, biocompatible liquid phase containing sterile thrombin and a solid phase of biocompatible polymer particles homogeneously dispersed in the liquid phase (claim 1), and a method of making same (claim 8).

Reich et al. invariably disclose dried hemoactive materials comprising a dried, cross-linked biologically compatible polymer. Reich et al. clearly state:

> According to the present invention, hemoactive materials comprise a dried, cross-linked biologically compatible polymer which forms a hydrogel when exposed to blood and a non-cross-linked biologically compatible polymer which solubilizes when exposed to blood. A cross-linked polymer is dispersed in a dried matrix of the non-cross-linked polymer, and the materials are delivered to surgical sites, wounds, and other target regions in tissue which are subject to bleeding or otherwise have blood present ([0012], page 1; emphasis added).

The Reich et al. materials can be formed into sheets ([0012], page 1), powders, pellets, large blocks, plugs, cylinders, tubes, split tubes, or other forms ([0012], page 2). Reich et al. fail to disclose or suggest that their compositions can be in the form of a homogeneous dispersion of biocompatible polymer particles in a continuous liquid phase containing sterile thrombin, as claimed herein. Reich et al. disclose only sterilized solid compositions.

> Usually, the compositions will be in the form of a sheet, typically having a thickness in the range from 1 mm to 25 mm, preferably from 2 mm to 15 mm. Alternatively, the materials can be formed into powders, pellets, large blocks, plugs, cylinders, tubes, split tubes, or other forms which may be

> conveniently delivered or placed to target tissue sites. (Reich et al., [0012], page 2, middle of paragraph).

The Examiner directs attention to paragraph [0021] for the proposition that Reich et al. disclose sterilizing liquid compositions. However, a fair and complete reading of paragraph [0021] reveals that after forming a liquid composition of the dissolved, non-cross-linked polymer and the dispersed cross-linked polymer, Reich et al. dry the composition to a solid phase form.

> Particles of cross-linked biologically compatible polymer as described above are then suspended in the aqueous medium. The aqueous medium is then dried to form a solid phase comprising the dried polymeric particles in a dry matrix of the non-cross-linked polymer. Lyophilization (freeze-drying) is the preferred drying technique, although air drying, heat-assisted drying, spray drying, molding, and other methods could also be used under certain circumstances. (Emphasis added).

Reich et al. never disclose sterilization of their liquid, intermediate composition; as such, the intermediate, liquid composition cannot comprise "sterile thrombin", as claimed herein, and cannot therefore anticipate the present claims.

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Verdegaal Bros. V. Union Oil Co. of California, 814 F2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Withdrawal of the rejection is requested on this basis.

> Instead, Reich et al. disclose sterilization of "dried polymeric materials".

> Referring now to FIG. 3, kits according to the present invention will comprise a sheet 10 or other form of the dried polymeric material of the present invention, such as pellets 12, plugs 14, or the like. The materials will be formed sterilely or will be sterilized, preferably by terminal sterilization using γ-irradiation, ethylene oxide, electronic beam irradiation, and the like. While still in a sterile form, the materials will be packaged in a

> sterile package 20, such as a pouch, tube, tray, box, or the like. Instructions for use setting forth a method of placing the material over tissue in the presence of blood, e.g., at a wound, or surgical site, will also be provided as part of the kit. (Paragraph [0041], emphasis added).

Applicants respectfully submit that Reich et al. fails to anticipate the presently claimed invention.

In maintaining the rejection from the prior Office Action, the Examiner states:

> The method of preparing the instant composition does not necessarily require sterilization of the liquid either but sterilization of the whole composition, note instant claim 8, of page 12, line 8. Applicants' claims do not omit sterilization of the composition as a whole at least as the claims read now. (Final Office Action, page 4, middle).

Applicants fail to understand the relevance of the Examiner's comment.

Applicants do claim sterilization of the "whole composition"; however, the "whole composition" is in the liquid state, i.e. it has a continuous phase of liquid. This the prior art fails to disclose or even suggest.

The Examiner's rejection relies upon reading disparate, unrelated portions of the Reich et al. reference together. Such "picking and choosing" is not permitted within the purview of the patent law as to anticipation.

> [R]ejections under 35 U.S.C. 102 are proper only when the claimed subject matter is identically disclosed or described in "the prior art"...[so as to] direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference...There is nothing in the teachings relied upon by the Patent Office which "clearly and unequivocally" directs those skilled in the art to make this selection nor any indication that [patentee] ever made the selection himself. In re Arkley, Eardley and Long, 172 USPQ 524, 526 (CCPA 1972); emphasis added.

Reich et al. never disclose or suggest sterilizing a liquid composition containing thrombin, let alone containing thrombin AND biocompatible polymer particles.

> It is not sufficient that each element be found somewhere in the reference, the elements must be "arranged as in the claim." Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 730 F.2d 1452, 1458 (Fed. Cir. 1984).

Clearly there is no identity of subject matter between Reich et al. and the present claims. Withdrawal of the rejection is requested.

Further, no rejection under 35 U.S.C. §103 would be proper over Reich et al. Applicants disclose known problems with trying to sterilize thrombin:

> ...as thrombin is known to be denatured by exposure to sterilizing condition such as ionizing radiation conventionally used to sterilize the powders, which denaturing destroys all enzymatic activity of the thrombin, thrombin has not been reported to be incorporated into the hemostatic compositions and then terminally sterilized prior to use to ensure a sterile composition. In fact, when thrombin is used in conventional hemostatic compositions, nonsterilized thrombin is added after sterilization of hemostatic composition. (Specification, page 2, lines 2-8; emphasis added).

Reich et al. apparently fail to appreciate this difficulty.

The examples (pp. 7-9) of the present application support this problem, and Applicants' solution thereto. The data reveal that an unsterilized thrombin/saline combination (Ex. 1a) loses 90.8% activity after 30 days (Table 1), whereas a sterilized version of the same combination (Ex. 1b) loses 100% activity within 6 days (Table 2), both in the absence of the claimed biocompatible polymer particles. The additional data demonstrate the efficacy of the claimed invention.

In view of the foregoing, it is respectfully submitted that the present claims are in condition for allowance. Prompt notification of allowance is respectfully requested.

Respectfully submitted,

Date: March 26, 2009

Michael J. Mlotkowski
Attorney for Applicants
Registration No. 33,020
(703) 584-3270

POST OFFICE ADDRESS to which
Correspondence is to be sent:

Roberts, Mlotkowski, Safran & Cole
P.O. Box 10064
McLean, VA 22102